The invention also provides a dosage form comprising a medicant, said dosage form prepared by molding a flowable material, said dosage form having no more than one axis symmetry and being substantially free visible defects.

Brief Description of the Drawings

Figures 1A and 1B are examples of dosage forms made according to the invention.

Figure 2 is a flow chart of an embodiment of the method of the invention.

Figure 3 is a plan view, partially schematic, of a system for manufacturing dosage forms according to the invention.

Figure 4 is an elevational view of the system shown in Figure 3.

Figure 5 is a three dimensional view of a compression module and transfer device according to the invention.

Figure 6 is top view of a portion of the compression module shown in Figure 5.

Figure 7 depicts the path of one row of punches of a compression module during a revolution of the compression module.

Figure 8 depicts the path of another row of punches of the compression module during a revolution of the compression module.

Figure 9 is a partial cross-section of a compression module during compression.

Figure 10 is a cross-section taken through line 10-10 of Figure 9.

Figure 11 is a cross-section taken through line 11-11 of Figure 10.

Figure 12 is an enlarged view of the die cavity area circled in Figure 11.

Figure 12A shows another embodiment of a die cavity of the compression module.

Figure 13 is a top view of the fill zone of the compression module.

Figure 14 is a cross-sectional view of a portion of the fill zone of the compression module.

Figure 15 is a cross section taken through line 15-15 of Figure 6.

Figure 16 is a view taken along an arc of the compression module during compression.

Figures 17A-C illustrate one embodiment of a "C" frame for the compression rollers.

Figures 18A-C illustrate another embodiment of a "C" frame for the compression rollers.

Figures 19A-C illustrate a preferred embodiment of a "C" frame for the compression rollers.

Figure 20 is a top view of the purge zone and the fill zone of the compression module.

Figure 21 is a cross-section taken through line 21-21 of Figure 20.

Figure 22 is a cross-section taken through line 22-22 of Figure 20.

Figure 23 illustrates an embodiment of a powder recovery system for the compression module.

Figure 24 is a cross-section taken along line 24-24 of Figure 23.

Figure 25 shows an alternative embodiment of a powder recovery system for the compression module.

Figures 26A-C illustrate one embodiment of a thermal cycle molding module according to the invention in which dosage forms per se are made.

Figures 27A-C illustrate another embodiment of a thermal cycle molding module in which a coating is applied to a substrate.

Figures 28A-C illustrate a preferred embodiment of a thermal cycle molding module in which a coating is applied to a substrate.

Figure 29 is a three dimensional view of a thermal cycle molding module according to the invention.

Figure 30 depicts a series of center mold assemblies in a thermal cycle molding module.

Figure 31 is a cross-section taken along line 31-31 of Figure 30.

Figures 32-35 depict the opening, rotation and closing of the center mold assembly with the lower retainer and upper mold assembly.

Figures 36 and 37 are cross-sectional views of a lower retainer of a thermal cycle molding module.

Figure 38 and 39 are top views of an elastomeric collet of a lower retainer.

Figure 40 shows a preferred cam system for the center mold assembly of the thermal molding module.

Figure 41 is a cross-section of the center mold assembly showing one embodiment of a valve actuator assembly therefor.

The thermal setting molding module 400 is a rotary apparatus comprising multiple hot injection nozzles and cold molding chambers. Each molding chamber has its own nozzle. Advantageously, the volume of the molding chambers is adjustable.

In a preferred embodiment of the invention, the thermal setting molding module is used to make inserts for dosage forms. The inserts can be made in any shape or size. For instance, irregularly shaped inserts (or dosage forms per se) can be made, that is shapes having no more than one axis of symmetry. Generally however, cylindrically shaped inserts are desired.

The inserts are formed by injecting a starting material in flowable form into the molding chamber. The starting material preferably comprises an medicant and a thermal setting material at a temperature above the melting point of the thermal setting material but below the decomposition temperature of the medicant. The starting material is cooled and solidifies in the molding chamber into a shaped pellet (i.e., having the shape of the mold). Injection and molding of the inserts preferably occurs as the thermal setting molding module 400 rotates. In a particularly preferred embodiment of the invention, a transfer device 700 (as described above) transfers shaped pellets from the thermal setting molding module to a compression module 100 (also described above) as generally shown in Figure 2, to embed the shaped pellets into a volume of powder before such powder is compressed into a dosage form in the compression module.

The starting material must be in flowable form. For example, it may comprise solid particles suspended in a molten matrix, for example a polymer matrix. The starting material may be completely molten or in the form of a paste. The starting material may comprise a medicant dissolved in a molten material. Alternatively, the starting material may be made by dissolving a solid in a solvent, which solvent is then evaporated from the starting material after it has been molded.

The starting material may comprise any edible material which is desirable to incorporate into a shaped form, including medicants, nutritionals, vitamins, minerals, flavors, sweeteners, and the like. Preferably, the starting material comprises a medicant and a thermal setting material. The thermal setting material may be any edible material that is flowable at a temperature between about 37 and about 120°C, and that is a solid at a temperature between about 0 and about35°C. Preferred thermal setting materials include water-soluble polymers such as polyalkylene glycols, polyethylene oxides and derivatives, and sucrose esters; fats such as cocoa butter, hydrogenated vegetable oil such as palm

Preferably, the pistons 434 are adjustably controlled by the position of cam follower 470 and associated cam track 468. Pistons 434 are attached to piston attachment block 436 by suitable mechanical means so that pistons 434 move with piston attachment block 436. Piston attachment block 436 slides along the shafts 464 up and down. Preferably, there are two shafts 464 as shown in Figure 86. Mounted to piston attachment block 436 is cam follower 470. One or more springs 466 bias piston attachment block 436 and therefore pistons 434 into the inject position as viewed in Figure 85C. As thermal setting mold assembly 420 travels with rotor 402, cam follower 468 riding in its cam track actuates pistons 434 into the eject position, which empties the molding chamber in preparation for the next cycle (Figure 85D).

Accordingly, during operation of the thermal setting molding module 400, nozzles 410 move up during rotation of the thermal setting molding module 400 and inject a starting material into molding chambers 422. Next, starting material is hardened within the molding chambers 422 into shaped pellets. Nozzles 410 are then retracted from the molding chambers. All of this occurs as the molding chambers 422 and nozzles 410 are rotating. After the starting material has hardened into shaped pellets, it is ejected from the molding chambers. See Figures 87 and 88.

When used with a transfer device 700 according to the invention, the transfer device 700 rotates between the molding chambers 422 and plate 428. The retainers 330 of the transfer device 700 receive the shaped pellets and transfers them to the another operating module, for example a compression module 100. In the case of coupling a thermal setting molding module 400 with a compression module 100 via a transfer device 700, transfer device 700 inserts a shaped pellet into each die cavity 132 after the fill zone 102 but before the compression zone 106 of the compression module. It will be appreciated that a linked thermal setting molding module 400, transfer device 700 and compression module 100 are synchronized so that a shaped pellet is placed into each die cavity 132. The process is a continuous one of forming shaped pellets, transferring the shaped pellets, and inserting the shaped pellets.

The thermal setting molding module has several unique features. One is the ability to mass produce shaped pellets relatively rapidly, in particular molded dosage forms comprising polymers that are typically solids or solid-like between about 0 and about 35°C. The thermal setting molding module accomplishes this is by heating the

starting material prior to injecting it into the molding chambers and then cooling the starting material after injection.

Another unique feature of the thermal setting molding module is the adjustable volume of the molding chambers. Adjustability and tuning of volume and therefore weight is especially advantageous for the production of shaped pellets comprising high potency or highly concentrated drugs, which are dosed in small amounts. Another advantage of the thermal setting molding module is that it can employ liquids. Unlike a particulate solid, such as powders typically used to make dosage forms, the volume of a liquid is relatively invariable at constant temperature. Density variations, which are troublesome in powder compression, are therefore avoided with liquids. Very accurate weights, especially at very low weights (i.e. with starting materials comprising high potency medicants) are achievable. Moreover, blend uniformity is also less assured with solid powders. Powder beds tend to segregate based on differences in particle size, shape, and density.

Another advantage of the thermal setting molding module is that it molds starting material while continuously rotating. This permits its integration with other continuously operating rotary devices, resulting in a continuous process. Conventional molding operations are typically stationary and have one nozzle feeding multiple mold cavities. Runners are often formed using in conventional equipment. By providing a nozzle for each molding chamber, runners are eliminated. Preferably, one control valve controls multiple nozzles. This simplifies the design of the thermal setting molding module, reducing cost. The thermal setting molding module may, of course be designed to operate without rotation of the rotor, for example on an indexing basis whereby a stationary group of nozzles engages molding chambers on a indexing rotary turn table or a linear recalculating indexing belt or platen system. However, by using a rotary system higher output rates can be achieved since products are continuously produced.

Specific embodiments of the present invention are illustrated by way of the following examples. This invention is not confined to the specific limitations set forth in these examples, but rather to the scope of the appended claims. Unless otherwise stated, the percentages and ratios given below are by weight.

In the examples, measurements were made as follows.